Program/Abstract # 106
Fibroblast growth factor signaling in skeletal evolution
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The genetic basis of morphological variation has been a long lasting question in biology both within and between species. We are using a forward genetic approach in zebrafish to investigate this question. As part of a large-scale screen, we isolated a mutant, *spiegeldanio* (*spd*), which displayed a scale-loss phenotype similar to variation seen in other fish species. We positionally cloned *spd* and found a missense mutation in the kinase domain of the *fibroblast growth factor receptor 1* (*fgfr1*) gene. The specificity of *fgf* signaling in vertebrate development is thought to arise from genome duplications and expansion of paralogues with unique developmental functions. Consistent with this, we find a second, uncharacterized, paralogue of *fgfr1* (*fgfr1b*) in zebrafish confirming the duplication of this gene in teleosts. Due to the phenotypic similarity between *spd* and the mirror carp (*C. Carpio*), we cloned *fgfr1a* from the carp. We show that the mirror carp phenotype is due to mutations in the kinase domain of one *fgfr1a* paralogue. We next sought a case of naturally occurring scale-loss. The *Phoxinellus* genus is a naturally occurring species in which scale-loss is a defining, derived trait for the genus. We found a consistent amino acid change in *fgfr1a* in two *Phoxinellus* species compared to the scaled outgroup, *Telestes*. We are testing the causation of this change by genetic sweep analysis and functional rescue in zebrafish *spd* mutants. These two cases support the utility of using forward genetics to identify genes involved in evolutionary change.

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Program/Abstract # 107
Exploring the developmental and evolutionary relationship between cardiac and blood/endothelial precursors
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nkx2.5 and *nkx2.7* are the NKX2 family members expressed in cardiac tissue in zebrafish. Both genes are expressed in the anterior lateral plate mesoderm (ALPM) during gastrulation in overlapping but distinct expression domains: *nkx2.7* is expressed throughout the ALPM, which is known to give rise to blood, endothelial and cardiac tissues, while *nkx2.5* is restricted to the heart region. Here we show that the most anterior region of the ALPM has a latent cardiac potential. We show that knocking down *nkx2.7* in the zebrafish embryo leads to ectopic expression of *nkx2.5* in the most rostral ALPM territory. In an *nkx2.7* deficient embryo, early cardiac genes are now expressed at the expense of key regulators of blood/endothelial fate (*scl*, *etsrp* and *pu.1*). In addition, when *nkx2.5* is overexpressed these main hematopoietic and vasculogenic players are affected, revealing *nkx2.5* as a repressor for the blood/endothelial programs. In this study we show that a latent embryonic potentiality to form blood/endothelial or cardiac tissue is present throughout the ALPM, placing *nkx2.7* as a territory boundary modulator. We also present evidence that an important embryonic signal for this boundary modulation is fibroblast growth factor. Taken together our data suggest an elegant crosstalk in the ALPM in a manner that limits heart size. These data, together with recently published results, suggest that the blood/endothelial precursors in this region may represent evolutionary antecedents of the second heart field in higher vertebrates.

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Program/Abstract # 108
Targeted disruption of the *Mohawk* homeobox gene results in tendon defects in mice
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The *Mohawk* gene encodes a new TALE-class atypical homeodomain protein with its homeodomain exhibiting the highest similarity to those of the Irx subfamily. *Mohawk* mRNA is abundantly expressed and highly regulated during mouse craniofacial and musculoskeletal development. To investigate the role of this putative transcription factor in mouse development, we generated mice with a conditional null mutation in the *Mohawk* gene. We found that *Mohawk* null mutant mice are viable and fertile, but exhibit a wavy or curly tail phenotype. Further characterization revealed that *Mohawk* null mice have hypoplastic tendons in the tail and limbs. In addition, we found that the expression of *Scleraxis*, which encodes a transcription factor required for tendon development, is upregulated in *Mohawk* mutant mice, indicating that *Mohawk* interacts with *Scleraxis* to regulate tendon development.

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Program/Abstract # 109
Persistent expression of Pax3 in neural crest causes cleft palate and defective osteogenesis
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Developmentally critical transcription factors regulate tissue patterning and cell fate determination. Upon differentiation, expression of early regulators frequently abates, suggesting that they may also play a role in maintaining an undifferentiated phenotype. Pax3 is required for proper development of multiple neural crest lineages and for activation of lineage-specific programs, yet expression is generally extinguished once neural crest cells migrate from the dorsal neural tube and begin to differentiate. We asked whether persistent Pax3 expression in neural crest derivatives of Pax3-expressing precursors would affect development or patterning. Our results demonstrate that persistent expression of Pax3 in cranial neural crest cells results in cleft palate and additional craniofacial defects. Further, our results suggest that Pax3 normally functions to directly regulate and maintain expression of Sostdc1, an inhibitor of bone morphogenetic protein (BMP) signaling. Cranial crest expressing persistent Pax3 is resistant to